DIFFUSE GLIOSIS OF THE CEREBRAL WHITE MATTER IN A CHILD.

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The case here reported was that of a child which, after a fall on the back of the head, gradually lost power to walk, grew deaf, dumb, blind, and stupid, and died twelve months after the fall. The autopsy showed a peculiar overgrowth of neuroglia, with some destructive properties, confined to the white matter of the posterior parts of the cerebrum, optic thalami, and areas in the white matter of the cerebellum.

I. CLINICAL HISTORY.

Dr. Bullard.

Edward J., six years old, born in Boston, was first seen January 16. 1904.

There was no history of inheritance. Parents were healthy. There were ten children, patient being the eighth. Of these five were dead, four of "stomach trouble" and one of "meningitis."

The patient had always been well up to the time of the present trouble, except for measles when three years old.

Present trouble: Six months ago while playing in the cellar he fell backward down three steps. He was not unconscious, but got up himself and came up stairs crying. He seems to have had some nose-bleed, and possibly bleeding from one ear. The night following he was feverish and restless, but not apparently delirious. The next day he seemed well, and went out to play as usual. He did, however, have nose-bleed whenever his face was washed.

Since the accident he has been "nervous," and for five months he has had some difficulty in walking, staggering so that he is obliged to put out his hands to steady himself. Has never fallen from this cause. Can use his knife and fork. Mother thinks he is becoming stupid. Frequency of micturition. Is very deaf and has been taken to the Eye and Ear Infirmary, where operation for adenoids was advised.

Physical examination: Same as before, but now he obeys no directions and does not appear to understand or notice what is going on about him. Cries when examined. Walks with very short steps swaying from side to side.

Dr. Holmes (Aural Department) reports: No aural signs to account for the deafness, which is apparently of nerve origin.

July 6. Dr. Williams (Eye Department) reports: Some atrophy of each optic nerve, but not enough to account for almost total lack of vision. The latter is presumably of cerebral origin.

July 13. Was admitted to the Hospital Second Surgical Service, Dr. Monks. Temperature normal. Pulse 100-120.

July 18. Operation. Dr. Monks. Trephined about 1½ inch behind and 1 inch above right ear. Dura thickened. No visible cerebral pulsation. Dura opened. Pia slightly thickened, edematous. Several drachms of clear amber-colored fluid drawn from lateral ventricle.

July 20. Died.

II. ANATOMICAL FINDINGS.

Permission was granted to open the cranial cavity. The examination was made fifteen hours after death by Dr. R. L. Thompson, whom we wish to thank for his record. The child was 129 cm. long. Development fair. Nutrition good. Pupils equal, 5 mm. wide. Circumference of skull 53 cm. Frontal suture well marked. Surgical opening 1 cm. square in squamous portion of right temporal bone, 5 cm. above and behind external auditory meatus. Dura everywhere adherent to calvarium.

Brain with pia mater weighs 1,445 gms. Pia mater and vessels normal. Convolutions symmetrical. Substance very firm toward occiput. Ventricles contain a normal amount of fluid tinged with blood. Cruor clot, 2 cm. in diameter, in descending horn of right ventricle.

The white matter of the posterior part of the centrum semiovale in both hemispheres is replaced with grayish or straw-colored slightly translucent material of a dense consistence. The lesion is somewhat sharply limited to the white matter; the cortex, of a paler color, sinks below the surface of section. In the right occipital region there is a narrow layer of less dense white matter between cortex and lesion.

The areas of increased density were roughly marked out at autopsy. On the right the lesion involves and in part replaces the white matter of the occipital, parietal, and temporal lobes. The right optic thalamus is somewhat firmer than normal. In the left hemisphere the lesion is still more marked and almost everywhere replaces the white matter of the occipital, parietal and temporal lobes. The left optic thalamus is even firmer than the right. The lesion on the left side stretches at least 1 cm. anterior to a frontal plane taken just in front of optic thalamus. Pieces were removed for fixation in Zenker's fluid, and the rest of the brain was hardened in 10 per cent. formaldehyde.

III. MICROSCOPIC FINDINGS.

The sclerosis of the cerebral substance preserves on microscopic examination the same remarkable limitation to the central white matter which was noted in the gross. Except in the optic thalami, the limits of the white matter are nowhere transgressed by the neuroglia overgrowth. The exterior of the lesion in some parts of the occipital region follows the contour, and coincides precisely with the inner limits of gray matter. But, in general, the sclerosis corresponds rather to the body of white matter known as the centrum semiovale and may spare the intragyral portion of the white matter.

In spite of the massive character of the lesion, and the compactness of many portions of its structure, the overlying cortex fails to show major lesions, such as secondary changes in nerve cells due to the loss of their processes, or accumulations of phagocytic cells in vessel sheaths, or a reaction on the part of the neuroglia. It is noteworthy that even the upper or subpial layer fails to show a reaction on the part of the neuroglia, despite the frequency of this reaction under numerous conditions. The pia mater and its vessels are likewise free from lesion.

The extent and nature of the damage done by the lesion cannot be exactly determined. The volume of brain tissue remains unaltered or has been slightly increased by the lesion. There has been at some time considerable destruction or alteration of tissue in the region, as is shown by dense deep masses of pigment-bearing phagocytic cells in the sheaths of the appertaining vessels. The myelin sheaths, and doubtless numerous axis cylinders, have been destroyed in the area of sclerosis. In certain areas which seem paved with neuroglia giant cells separted by a few delicate neuroglia fibrils, it is certain that the original elements must have been destroyed.

In other parts it is by no means certain that all or even the majority of the axis cylinders have been dissolved in the lesion. In a preparation stained with phosphotungstic acid hematein (Mallory) it is possible to follow certain myelinated fibers, in whose myelin sheaths a delicate skeletal substance may stain, till the fibers enter the sclerotic area and lose their myelin. Neither myelin nor the delicate substance within the sheath can be demonstrated in quantity within the sclerotic area.

The anilin blue stain (Mallory) for connective tissue is of service on this point. It is possible for instance, to demonstrate in this case, by means of the anilin blue stain, the secondary degeneration of fiber bundles about the Gasserian ganglion and the secondary degeneration of most of the central bundles of the optic nerve. Unfortunately the application of the anilin blue stain to the brain substance of this case is of less service. For it proves not possible to differentiate convincingly the supposed axis-cylinders from long cell processes of some of the large active neuroglia cells which characterize many parts of the sclerotic regions. However, so far as appearance without differential staining can convince, it is possible to say that at least some axis cylinders, minus myelin, penetrate the sclerotic areas. This would align the case with the cases known as multiple sclerosis.

The finer characters of the lesion are of interest, especially as bearing on the differentiation of gliosis from glioma.

The sclerotic tissue varies strikingly in microscopic structure, although the amount of intercellular substance is everywhere above that of the normal cerebral white matter. The variations are chiefly shown in the number and character of the neuroglia cells which produce the fibrils. The transitions in the mass of the lesion are never abrupt and never so well marked as the transition between the sclerotic tissue and the relatively normal cortex. The neuroglia cells vary in number and size in the sclerotic tissue, just as they do in those focal overgrowths of neuroglia tissue which we know as glimata.

In places (characteristically along the exterior of the sclerotic tissue), the cells are small, placed at fairly regular intervals, and provided with branched cell-bodies which somewhat recall the characteristic cell bodies of reacting sub-pial neuroglia cells.

In other places (characteristically in the interior of the lesion), the cells are larger (often meriting the name giant cell), placed at smaller intervals (sometimes giving a pavemented appearance to the lesion), and provided with numerous overlapping nuclei which are crowded about the periphery of the cell. The centers of these large cells are homogeneous and finely granular and are provided with a varying number of centrosome-like structures.

In a few foci, there is a third type of cell in which activity seems to be spent on expansion of the cell-body and the production of numerous heavy, branched, and deeply staining processes, which are sometimes frayed at the ends like cut wire-rope.

In places there are remarkable clusters and rows of ependymal cysts, lined with perfectly formed ependymal cells, which are provided with basal bodies and attached cilium-like appendages. These cysts are not of diffuse occurrence but occur particularly in the neighborhood of the posterior horns of the ventricles. Occasionally the cysts are so aligned, between stratified masses of neuroglia coincident in direction with the major axis of the ventricle, that the impression is gained that such accessory cystic spaces are developed along with the ventricle and belong to its ground plan.

Over against these perfectly formed ependymal cysts may be set certain less regular cysts which are perhaps due to the hollowing out of the cytoplasm of some of the giant cells with peripheral nuclei noted above. Such irregular cystic spaces are, however, not common in this tissue.

The gradual variations in cell character above noted, taken together with certain variations in the amount and texture of the intercellular fibrillary substance (often particularly dense about vessels), are not inconsistent with the diagnosis, glioma. There is considerable evidence of tissue destruction throughout the sclerotic tissue in the shape of dense deep masses of pigment-bearing phagocytic cells in the vessel sheaths. The material so laid down is probably derived from the destruction of nerve fibre constituents incident to the lesion, since there is nowhere any sign of necrosis in the sclerotic tissue itself and there is little or no accumulation of phagocytic cells in the overlying cortex or in the pia mater.

IV. SUMMARY.

1. Boy of six and a half years. Measles at three years. One year before death, fell backward down three steps in a cellar, with epistaxis, and possibly bleeding from ear. Afterward "nervous." A month later began to stagger in walking, became gradually deaf and stupid, later blind and dumb. Operation for chronic internal hydrocephalus. Death two days after operation.

2. The autopsy showed sclerosis of the white matter of the occipital, parietal, and temporal lobes on both sides with sclerosis of optic thalami and of small, roughly symmetrical areas in the white matter of the cerebellum.

3. The microscopic examination shows a cellular and fibrillary overgrowth of neuroglia, sharply limited to the white matter. The picture gradually varies from that of masses containing giant cells and few fibrils to that of active fibril-producing cell masses or that of stratified areas of inactive fibrillar gliosis.

4. The lesion involves the destruction of myelin sheaths and considerable axis-cylinder material. The lesion may be described as a multiform gliosis of the white matter with extensive mildly destructive properties. The nutrition of the areas is maintained. The overgrowth of neuroglia substitutes for, and to some extent destroys, the involved tissues, but fails to invade, in the sense of invasion by glioma. The overlying cortex fails to show important changes. The origin of the condition is unknown.